Notice of Allowability	Application No.	Applicant(s)	
	10/601,345	UITTERLINDEN ET AL.	
	Examiner	Art Unit	
	Katherine Salmon	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☐ This communication is responsive to _____.

2. ☒ The allowed claim(s) is/are *6,9-12,29 and 30*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *10252007* .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

1. An extension of time under 37 CFR 1.136(a) is required in order to make an examiner's amendment which places this application in condition for allowance. During a telephone conversation conducted on 10/24/2007, Darla Yoerg requested an extension of time for 1 MONTH(S) and authorized the Director to charge Deposit Account No. 19-1970 the required fee of $60.00 for this extension and authorized the following examiner's amendment. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

3. Authorization for this examiner's amendment was given in a telephone interview with Darla Yoerg (attached is Examiner initiated Interview Summary).

The application has been amended as follows:

Claim 6. A method of determining susceptibility to vertebral bone mineral density (BMD)-independent fracture in a Caucasian female subject, the subject comprising:

(i) at least one estrogen receptor α gene comprising a PvuII site and a XbaI site, wherein the PvuII site can exist as a P or p allelic form, and the XbaI site can exist as an X or x allelic form; and
(ii) a vitamin D receptor gene, wherein the vitamin D receptor gene comprises a BsmI site, an ApaI site and a TaqI site, wherein the BsmI site can exist as a B or b allelic form, the ApaI site can exist as an A or a allelic form, and the TaqI site can exist as a T or t allelic form,
said method comprising analyzing nucleic acid molecules obtained from the subject to determine which of the P, p, X, and x alleles of the estrogen receptor α gene are present, and further comprising determining the copy number of a member of the group consisting of the B, b, A, a, T and t alleles of the vitamin D receptor gene, wherein the presence of a haplotype comprising the p and x alleles of the estrogen receptor a gene and a homozygous haplotype comprising the baT alleles of the vitamin D receptor gene is indicative of an increased susceptibility to vertebral BMD-independent fracture.

Claim 8. Cancelled

Claim 9. A method according to claim 6, wherein said method is performed on a blood or tissue sample of the subject.

Claim 12. A method of treating a Caucasian female subject to reduce the risk of vertebral bone mineral density (BMD)-independent fracture, wherein the subject comprises:

(i) at least one estrogen receptor α gene comprising a PvuII site and a XbaI site, wherein the PvuII site can exist as a P or p allelic form, and the XbaI site can exist as an X or x allelic form; and
(ii) a vitamin D receptor gene, wherein the vitamin D receptor gene comprises a BsmI site, an ApaI site and a TaqI site, wherein the BsmI site can exist as a B or b allelic form, the ApaI site can exist as an A or a allelic form, and the TaqI site can exist as a T or t allelic form, wherein the presence of a haplotype comprising the p and x alleles of the estrogen receptor gene and a homozygous haplotype comprising the baT alleles of the vitamin D receptor gene is indicative of an increased susceptibility to vertebral BMD-independent fracture,
said method comprising determining whether the px haplotype of the estrogen receptor α gene and the homozygous baT haplotype of the vitamin D receptor gene are present in said subject, and treating the subject to reduce the risk of vertebral BMD-independent fracture if the subject has both said haplotypes, wherein the treatment comprises at least one treatment selected from the group consisting of modifications to lifestyle, regular exercise, changes in diet and administration of a pharmaceutical preparation effective to reduce the risk of vertebral BMD-independent fracture.

Claim 21 Cancelled.

Claim 24 Cancelled.

Claims 34-36 Cancelled.

4. The following is an examiner's statement of reasons for allowance:

Claims 6, 9-12 and 29-30 are allowable.

The claims are drawn to a method of determining susceptibility to vertebral bone mineral density independent fracture in a Caucasian female subject comprising detecting that the p and x alleles of the estrogen receptor α gene and the homozygous haplotype of the baT alleles of the vitamin D receptor gene are present, wherein the detection of the combination of alleles is indicative of an increased susceptibility to vertebral BMD-independent fracture. The claims are drawn to treating a Caucasian female subject to reduce the risk of vertebral BMD independent fractures comprising detecting that the p and x alleles of the estrogen receptor α gene and the homozygous haplotype of the baT alleles of the vitamin D receptor gene are present and treating with modifications to lifestyle, regular exercise, changes in diet or administration of a pharmaceutical preparation effect to reduce the risk of vertebral BMD-independent fracture.

The 35 USC 112/ Enablement in the Final Rejection mailed 1/22/2007 has been withdrawn based on the amendments to the claims. The claims as written specifically define the genotype correlated with vertebral bone mineral density independent fractures in a Caucasian female subject. Therefore, the enablement issues made of record in the Final Rejection mailed 1/22/2007 are moot.

Further, Claim 12 is now drawn to a method of treating a Caucasian female to reduce the risk of vertebral bone mineral density independent fracture comprising detecting the genotype and then treating the subject with a treatment selected from the group consisting of modifications to lifestyle, regular exercise, changes in diet and administration of a pharmaceutical preparation. The claim as written requires the detection of px and bbaaTT and then treating with known at the time of filing treatment methods to reduce the risk of vertebral bone mineral density independent fracture.

The instant specification teaches that there is an increased susceptibility to vertebral BMD independent fractures in Caucasian females with px allele and the homozygous haplotype comprising the baT alleles (p. 31 lines 5-10 and p. 32 lines 13-16).

Though, various genotypes of the estrogen receptor α gene and the vitamin D receptor gene are know in the art to be correlative with various types of fractures, the combination of the px allele and the homozygous haplotype comprising the baT allele in Caucasian females in vertebral BMD independent fractures had not been previously observed in the art. Because each combination of these alleles and the correlation to fracture type in various population types is unpredictable (as discussed in the 35 USC 112/ Enablement presented in the Final Rejection mailed 1/22/2007), it would not be obvious to correlate the specific genotype in Caucasian females to increased susceptibility to vertebral BMD-independent fractures. Thus the prior art neither teaches nor suggests the claimed invention and Claims 6, 9-12 and 29-30 are allowable.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine Salmon whose telephone number is (571) 272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Katherine Salmon
Examiner
Art Unit 1634

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER